MULTIMODALITY IMAGING OF THE PROSTATE

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Introduction

The thrust of cancer care today is patient-specific therapy that maximizes cancer control while minimizing the risk of complications. Imaging can contribute valuable information toward achieving such individualized therapy in patients with prostate cancer. Not only can it aid tumor detection, diagnosis, staging, and follow-up, it is also emerging as tool for predicting treatment response. The choice of imaging modality, however, must be tailored to the specific clinical questions that need to be addressed. This lecture will discuss the appropriate use of cross-sectional imaging modalities in prostate cancer care, giving particular attention to magnetic resonance (MR) imaging--the most sensitive and versatile modality for prostate cancer imaging.

Imaging Primary Prostate Cancer

Transrectal ultrasound (TRUS) is the standard modality used for biopsy guidance and brachytherapy seed placement. However, no consensus exists regarding the use of imaging for evaluating primary prostate cancer. Though TRUS is often used to measure the volume of the prostate gland, it is generally considered insufficient for local staging. Unlike TRUS, T2-weighted MR imaging shows the prostate zonal anatomy and surrounding structures in exquisite detail; furthermore, functional and metabolic imaging techniques can be added to conventional MR imaging for more precise prostate cancer evaluation.

Conventional MR Imaging

Optimal MR imaging for prostate cancer detection requires the use of an endorectal coil and a pelvic phased-array coil with a magnet of 1.5 Tesla or higher, thin (3-mm) slices, and a small (14-cm) field of view. On T2-weighted MR images, cancer usually appears as decreased signal intensity within the high-signal-intensity peripheral zone. MRI can also be used to detect prostate cancer in the transition zone (sensitivity, 75%-80%; specificity, 78%-87%); the features most significantly associated with the presence of transition zone cancer were homogeneous low T2 signal intensity and lenticular shape. Like prostate cancer, post-biopsy hemorrhage produces low signal intensity on T2-weighted images and can therefore complicate image interpretation. T1-weighted images can be used to detect post-biopsy intraglandular hemorrhage and reduce false positive findings. On T1-weighted images, post-biopsy hemorrhage is distinguishable by its high signal intensity relative to the low-to-intermediate signal intensity of the prostate.

MRI is useful for directing targeted biopsy, especially for patients with previous negative biopsy results yet persistently elevated prostate-specific antigen (PSA) levels; this situation occurs most often with lesions in the anterior peripheral, transition or central zones (i.e., regions not palpable by digital rectal examination (DRE) and not routinely sampled at biopsy). In a study comparing DRE, TRUS-guided biopsy and endorectal MRI in the detection and localization of prostate cancer, MRI performed significantly better than DRE in detecting cancer in the apex, mid-gland, and base, and significantly better than TRUS-guided biopsy in the mid gland and base. Furthermore, MRI was capable of detecting cancers in the anterior part of the gland. The use of MRI for biopsy planning may reduce false-negative biopsy results. Methods for fusing MRI with real-time TRUS for biopsy guidance are being explored and appear promising.

MRI can help determine the local stage of prostate cancer, as it can show laterality and contribute significant incremental value to clinical variables in predicting extracapsular extension and seminal vesicle invasion. Criteria for extracapsular extension on MRI include asymmetry of the neurovascular bundle (NVB); tumor envelopment of the NVB; an angulated prostate gland contour; an irregular or spiculated margin; obliteration of the rectoprostatic angle; capsular retraction; a tumor–capsule interface greater than 1 cm; and a breech of the capsule with evidence of direct tumor extension. In the evaluation of extracapsular extension, transaxial planes of section are essential and a combination of transaxial and coronal plane images is ideal. The use of sagittal plane images facilitates evaluation of tumor located at the apex.

Identifying extracapsular extension on MRI can be challenging, and accuracy in performing this task varies widely. However, a recent study showed that radiologists' skill in identifying extracapsular extension could be significantly increased through their participation in a dedicated, interactive training curriculum lasting less than three months. In the study, which included 11 radiology fellows, the fellows' average AUC for identifying extracapsular extension increased from 0.50 at the beginning of training to 0.81 at the end ($p<0.001$).

The criteria for seminal vesicle invasion on MRI include disruption or loss of the normal architecture of the seminal vesicle; focal or diffuse low signal intensity within the seminal vesicle; low signal intensity within the seminal vesicle causing mass effect; enlarged low-signal-intensity ejaculatory ducts; obliteration of the angle between the prostate and the seminal vesicle on sagittal images; and direct extension of the low signal intensity of tumor from the base of the prostate to the seminal vesicle.

Information from MRI may aid surgical planning. A study of 135 patients showed that review of endorectal MR images before radical prostatectomy improved the surgical decision to spare or resect the neurovascular bundles, especially in high-risk patients. However, another study found an elevated incidence of positive surgical margins in patients whose preoperative MRI studies erroneously indicated the absence of extracapsular extension.

Prostate MRI can also aid surgical planning by showing potentially metastatic regional lymph nodes. The standard criterion used to identify a metastatic lymph node is a short-axis diameter greater than 7-8 mm. This criterion has high specificity but low sensitivity, as metastases may be present in normal-sized nodes or absent in enlarged nodes. Lymphotropic nanoparticle–enhanced MRI, an investigational technique, has been found to yield sensitivity and specificity above 90% in the detection of prostate cancer lymph node metastases; it appears to allow identification of small metastatic lymph nodes

(<5 mm) and differentiation between benign reactive and malignant enlarged nodes. Although the technique is promising, a drawback is that the contrast agent must be administered the day before imaging.

The Added Benefits of Metabolic and Functional MR Imaging

Proton MR spectroscopic imaging (^{1}H-MRSI) can be performed on a standard 1.5-Tesla clinical scanner using commercially available software, after anatomical MR imaging is completed. ^{1}H-MRSI provides a 3-dimensional metabolic map of the prostate gland by displaying concentrations of the cellular metabolites citrate, creatine and choline, and polyamines. Normal peripheral zone prostate tissue contains high levels of citrate. Prostate cancer usually demonstrates elevated choline levels and diminished citrate, explained by a high phospholipid cell membrane turnover in the proliferating malignant tissue and a conversion from citrate-producing to citrate-oxidating cancer metabolism. Tumor detection is therefore based on the detection of an increased ratio of choline to citrate. With the latest software and improved spectral resolution, the polyamine signal can also be resolved. A decreased or absent polyamine peak adds to the specificity of prostate cancer detection on MRSI. In single-institution studies, the combination of MRI and ^{1}H-MRSI has shown excellent sensitivity and specificity for detecting cancer in the peripheral zone and can assist in prostate cancer staging and tumor volume estimation. In the evaluation of extracapsular extension, ^{1}H-MRSI may be particularly helpful for inexperienced readers of MRI.

Although the combination of MRI and ^{1}H-MRSI is mainly being used for high-risk patients, it may also have a role to play in patients with clinically low-risk disease. For example, MRI/^{1}H-MRSI in patients with clinical stage T1c prostate cancer may confirm the presence of small-volume disease or identify unexpected extracapsular extension. In one study, the addition of MRI or combined MRI/^{1}H-MRSI findings significantly improved the accuracy of clinical nomograms for predicting the presence of pathologically insignificant prostate cancer in patients with clinically low-risk disease; the improvement was greater with the use of combined MRI/1H-MRSI findings. A recent study also showed that MRI/^{1}H-MRSI contributed incremental value to clinical variables in predicting prostate cancer recurrence.

In dynamic contrast-enhanced MRI (DCE-MRI), sequential images are acquired during the passage of a contrast agent through a tissue of interest. DCE-MRI can be used to show differences in microvessel perfusion, permeability and extracellular leakage space. The relative peak enhancement in the peripheral zone of the prostate and the washout rate in the central gland are useful DCE-MRI parameters for detecting and localizing prostate cancer, and a number of single-institution studies suggest that DCE-MRI can add substantial value to conventional MRI in these tasks. For example, in a study assessing prostate cancer localization in 34 patients, the areas under the ROC curves (AUCs) for DCE-MRI and MRSI (0.91 and 0.81, respectively) were significantly higher than the AUC for T2-weighted imaging (0.68).

Diffusion-weighted MR imaging (DW-MRI) derives its image contrast from differences in the motion of water molecules between tissues. The motion of water molecules is more restricted in tissues with high cellular density associated with numerous intact cell membranes (e.g., tumor tissue). Visual assessment of the relative tissue signal attenuation at DW-MRI is being applied for tumor detection and characterization. Quantitative analysis of DW-MRI is achieved by calculating the apparent diffusion coefficients (ADCs) for all image pixels and displaying them as a parametric map. DW-MR images can be acquired quickly without administering a contrast agent.

On DW-MRI, prostate cancers usually have lower ADC values than normal peripheral zone, transition zone, and central zone tissue. However, the ADC values in prostate cancer and in prostatic tissue altered by benign processes overlap substantially. Single-institution studies have found that DW-MRI can significantly improve prostate cancer detection in the peripheral zone with T2-weighted imaging or MRSI and the estimation of prostate tumor volume with T2-weighted imaging.

Detection of Local Recurrence and Distant Metastases

When the PSA level rises after surgery or radiation therapy, MR imaging is useful in searching for local recurrence. MR imaging has proven to be superior to TRUS and CT in this task, especially in patients without palpable tumor in the prostatic fossa. Single-institution studies have suggested that DCE-MRI can facilitate detection of local recurrence in these settings.

Radionuclide bone scans and CT supplement clinical and biochemical evaluation for suspected metastasis when the PSA level is quite high. Guidelines for the use of bone scans (in patients with PSA > 10 ng/mL) and CT (in patients with PSA > 20 ng/mL) are often ignored, leading to overuse. Size criteria are employed to detect lymph node metastasis on both CT and MR imaging; these criteria have limited accuracy, as small metastatic nodes may be missed and large benign nodes mistaken for disease. As noted above, recent studies have shown that MR imaging with superparamagnetic nanoparticles, an investigational technique, has high sensitivity and specificity in detecting lymph node metastases.

Limited data suggest that FDG-PET/CT may have utility in the search for prostate cancer metastases after treatment, especially in aggressive and/or castration resistant disease. In a study of 91 patients with PSA relapse after radical prostatectomy, FDG PET appeared to be useful in patients with PSA > 2.4 ng/mL or PSA doubling time > 1.3 ng/mL/y. Although it detected locally recurrent or systemic cancer in only 28 patients (31%), it identified nearly all disease sites detected by CT or bone scanning. The authors therefore suggested that the combination of FDG PET (to detect systemic disease) and body MRI (to detect local recurrence) might provide a valuable imaging algorithm in appropriately selected patients with PSA relapse. PET/CT with ^{11}C-choline or ^{11}C-acetate appears promising for the assessment of nodal metastases before treatment as well as the detection of local recurrence and distant metastases.

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